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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/928,048	08/10/2001	Thomas L. Cantor		7860

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EXAMINER
COUNTS, GARY W

ART UNIT	PAPER NUMBER
1641	

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DATE MAILED: 02/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/928,048	CANTOR, THOMAS L.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9 and 17-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 17-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

The amendment filed 12/16/04 is acknowledged and has been entered.

Rejections withdrawn

The rejection of claims 1-9 and 19-25 as being vague and indefinite is withdrawn in view of the amendments to the claims.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-9 and 17-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. On page 5, second paragraph, lines 9-14 in the specification. The applicant discloses that in making a direct measurement of CIP, one can use an antibody or antibody fragment specific for a peptide sequence for CIP which by virtue of the unique CIP protein conformation is available for antibody binding but this same epitope is not available for antibody bind in CAP by virtue of the unique CAP protein conformation of CAP, in an amount sufficient to behind the CIP present, and thus, enable immunoassay measurement. Applicant's language is prophetic in nature and does not indicate that such a distinguishing antibody has been

produced at the time of filling. Applicant does not disclose an antibody that is able to distinguish a peptide sequence for CIP that present an epitope available for antibody binding in CIP, but does not bind to the same peptide sequence in cyclase activating parathyroid hormone. There is no description of an antibody in the specification that distinguishes a peptide sequence for CIP that presents an epitope on CIP and does not bind to CAP.

3. Claims 1-9 and 17-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. The factors that must be considered in determining undue experimentation are set forth in *In re W*ands USPTQ2d 14000. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The instant claims are directed to a method for measuring the amount of cyclase inhibiting parathyroid hormone (CIP) fragment in a sample by adding to the sample a first antibody or antibody fragment (or adding to a sample a labeled antibody or antibody

fragment) specific for a peptide sequence for cyclase inhibiting parathyroid hormone (CIP), but does not bind to this same peptide sequence in cyclase activating parathyroid hormone.

The disclose fails to teach an antibody that distinguishes a peptide sequence for CIP that present an epitope available for antibody binding in CIP, but does not bind to this same peptide sequence in cyclase activating parathyroid hormone. The instantly recited claims are totally dependent on the ability of the antibody to discriminate between the CIP presenting the epitope and the cyclase activating parathyroid hormone. Further, a search of the art indicates that such an antibody is not well known in the art. Also, applicants own statements in the specification indicate that such an antibody is not known in the art (For instance, on page 5, second paragraph, lines 9-21 in the specification. The applicant discloses that in making a direct measurement of CIP, one can use an antibody or antibody fragment specific for a peptide sequence for CIP which by virtue of the unique CIP protein conformation is available for antibody binding but this same epitope is not available for antibody bind in CAP by virtue of the unique CAP protein conformation of CAP, in an amount sufficient to behind the CIP present, and thus, enable immunoassay measurement. In other words, conformation changes between CAP and CIP do not make the CIP binding site available on CAP. Such a domain has been identified that functions in the opposite manner). Further, these antibodies are not well known in the art and thus one of ordinary skill in the art would have a low level of predictability in the art.

There are no working examples providing an antibody which distinguishes a peptide sequence for CIP that present an epitope available for antibody binding in CIP, but does not bind to this same peptide sequence in cyclase activating parathyroid hormone nor are there any working examples to provide guidance.

Because the disclosure fails to teach an antibody which distinguishes a peptide sequence for CIP that present an epitope available for antibody binding in CIP, but does not bind to this same peptide sequence in cyclase activating parathyroid hormone and because the art is unpredictable, such is not seen as sufficient to support the breath of the claims and one skilled in the art cannot practice the claimed invention without undue experimentation.

Response to Arguments

4. Applicant's arguments filed December 16, 2004 have been fully considered but they are not persuasive.

Rejections under 35 U.S. C. 112 first paragraph: Written Description.

Applicant traverses the written description rejection. Applicant directs Examiner's attention to In Enzo biochem. V. Gen-Probe, Inc., 323 F.3d 956,964 (Fed. Cir. 2002) in which the Federal Circuit cited the PTO Guidelines for the written description requirement. (p. 8, Remarks section). Applicant further directs Examiner's attention to In Noelle v. Lederman, 69 USPQ2d 1508, 1513-14 (Fed. Cir. 2004) in which the court relied upon *Enzo* when it stated that an applicant can claim an antibody by its binding affinity, "as long as an applicant has disclosed a "fully characterized antigen" either by its structure, formula, chemical name, or physical properties. Applicant states

that Applicant has described the antigen of interest, CIP by structure. These arguments are not persuasive because the fact patterns disclosed in In Enzo biochem. V. Gen-Probe, Inc., 323 F.3d 956,964 (Fed. Cir. 2002) and In Noelle v. Lederman, 69 USPQ2d 1508, 1513-14 (Fed. Cir. 2004) are different from that of the instant application. As stated above and in the previous office action the antibody of the current application discriminates between the CIP presenting the epitope and the cyclase activating parathyroid hormone and the Noelle antibody is not asked to distinguish between anything. Thus the instant application is different from Enzo and Noelle because the Applicant doesn't have the antibody and the existence of the antibody is unexpected.

Rejections under 35 U.S.C. 112 first paragraph: Enablement.

Applicant argues that Gao et al., demonstrates that it was within the skill in the art to produce antibodies that selectively bind to one peptide comprising hPTH or a fragment thereof while distinguishing other closely related peptides. Particularly, the Gao antibody that does not bind to hPTH-rp (1-86), yet recognizes the shorter peptide hPTH (1-84). This is not found persuasive because Gao et al is describing a different sequence (see also attached telephone interview of 02/10/05 in which Applicant stated that Gao et al was not of relevance because Gao et al teaches a different sequence).

Applicant states that an example of an antibody specifically binding a truncated form of PTH and not binding to the full-length peptide is described in D'Amour, et al, Clinical Chemistry 49: 12, pg. 2037-44 (2003) [Exhibit A]. D'Amour discloses a second form of PTH (1-84) that was not previous recognized. The new form of PTH (1-84) is recognized by antibodies that bind to the N-terminal region of PTH (1-84) (peak at

fractions 42-43 shown in CA-PTH assay in Figure 1). This new form of PTH (1-84) is not recognized by an antibody against the 15-20 region of PTH, which is the antibody used in the T-PTH assay (see the T-PTH assay in Figure 1 on page 2039). Applicant further directs Examiners attention to pages 2040 (left column) and 2041-2043. Applicant states that the T-PTH assay detects PTH (7-84), but does not detect or barely detects the newly discovered from of PTH (1-84). This is not found persuasive because D'Amour shows antibodies that did not react with a smaller fragment (19-84) (see p. 2040 left column). D'Amour suggests an epitope in the region (15-20). D'Amour is showing that hPTH (1-84) and hPTH (7-84) have an epitope in common. D'Amour is not showing that the antibody differentiates between hPTH (1-84) and hPTH (7-84). D'Amour is showing binding to a control having a region of 19-84. Further, the sandwich assays performed for CA-PTH assay and T-PTH assay would further suggest that another epitope is shared (p. 2042-2043). This is not found persuasive because as stated above the instantly recited claims are totally dependent on the ability of the antibody to discriminate between the CIP presenting the epitope and the cyclase activating parathyroid hormone and D'Amour hasn't shown antibodies which perform in this manner. Rather, D'Amour shows antibodies which bind to a control fragment 19-84.

Applicant argues that it was known in the art before this application was filed that it was possible to discriminate between closely related peptides, even in this same family of peptides, with an antibody. Antibodies that specifically bind to PTH peptides are the N-terminal, C-terminal and sequences in between were well known. Applicant

states that it was also well known that peptide antigens can comprises non-contiguous amino acids, and that the three-dimensional structure of a protein can bring distal groups together for from an antigen (Applicant directs Examiners attention of Rao, Exhibit B). Applicant further states that the production of antibodies that bind PTH (7-84) was clearly a routine matter when the application was filed, and antibody technology was described by the court as "well developed and mature". Applicant further states that since it was also known that differential binding analogous to that required for the claimed antibody could be activated, the systematic screening methods described in the specification would enable one of ordinary skill to select an appropriate antibody with which to practice the claimed invention. These arguments are not found persuasive because for reasons above and further because Applicant has not shown a single antibody that can discriminate between CIP and CAP and one cannot claim unexpected results without results and one of ordinary skill does not have the knowledge that there is a success and thus one of ordinary skill in the art would not expect to obtain an antibody that discriminates between CIP (7-84) and CAP (1-84).

Conclusion

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary Counts
Examiner
Art Unit 1641
February 14, 2005

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02/15/05